Mechanics and Regulation of Respiration

Introduction

The airway consists of two zones: a conducting zone and a respiratory zone. The respiratory zone is where gas exchange occurs. Within the alveoli, the air that has been brought in by the conducting zone undergoes gas exchange. Oxygen moves from the alveoli into red blood cells, and carbon dioxide moves from the blood to the alveoli. The details of this process are discussed in the next lesson. The conducting zone brings fresh air (rich in oxygen and poor in carbon dioxide) to the alveoli. After gas exchanged has occurred, the conducting zone carries out spent air (poor in oxygen and rich in carbon dioxide).

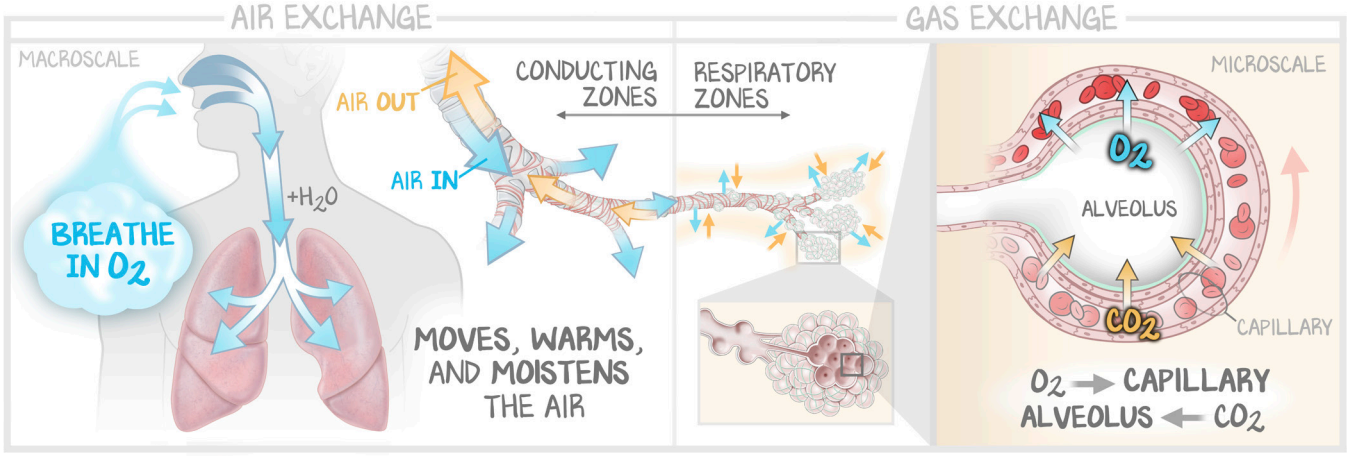

Figure 2.1: Gas Exchange vs. Air Exchange
Gas exchange is a microscopic process that occurs in the alveolus. Air equilibrates with the capillary, as oxygen enters the capillary and carbon dioxide exits the capillary. Air exchange is the macroscopic process that occurs through the rest of the airway.

Even though this lesson is about moving air through the conducting zone, the physiology focuses on the forces of the respiratory zone. When the alveoli open, air moves in. When the alveoli close, air moves out. There are forces that open alveoli, and there are forces that collapse alveoli. The forces that increase the size of the alveoli are the pull-forces of the elastic recoil of the chest wall, contraction of the diaphragm, and contraction of the accessory muscles of inspiration. Each of these pull-forces expands the alveoli. The forces that decrease the size of the alveoli are the inherent properties of the alveoli (their elastic recoil causes them to collapse), surface tension, and the push-forces coming from the accessory muscles of expiration. We're going to go through each, one at a time. These forces **cannot affect cartilaginous airways**, which means the trachea, bronchi, and terminal bronchioles are unaffected. In this discussion, therefore, the **alveoli** and **respiratory bronchioles** are the only part of the airway that matter.

Movement of Air, aka Alveolar Pressures

We will not discuss individual gases within the air for the remainder of this lesson. That means that when you see the word "pressure," we mean the force applied to air, and not the specific partial pressure of individual gases in the air. Specifically, you may recall that the total pressure of air at sea level is 760 mmHg. Yep, we're NOT doing that discussion. We are going to be discussing relative pressures. The atmosphere, air outside the human, is set at 0 cmH_2O. Any of the pressures listed for the rest of the lesson are relative to atmosphere, relative to 0 cmH_2O.

Back in physics in undergrad, you studied the **inverse relationship of pressure and volume**. If the volume of a container increases, the gas inside of it exerts a reduced pressure on the container. Uh-huh . . . Let's try this with simple lung mechanics. With something you can follow. Actually, do what the paragraph says as you read it. Take a really big breath and hold it. What happened? Your chest puffed up. Your lungs filled with air. Now, gently let it out. What happened? Your chest went back to normal. The air you had inhaled came out. This you can intuit—you suck air into your lungs to fill them; when you release your breath, air comes back out as your lungs deflate back to normal. So how did all that actually happen? **Air moves from higher pressure to lower pressure.**

When you took a big, deep breath, you used all of your muscles of inspiration. They all do the same thing—they open the alveoli. When those muscles contract, they pull on the chest wall, expanding it. The chest wall is attached to the pleural cavity, the pleural cavity to the alveoli, and the alveoli to all other alveoli. The contraction of inspiratory muscles expands the chest, pulls on the pleural cavity, and pulls open the alveoli—the volume of the alveoli increases. The increasing volume generates a negative pressure that sucks air into the alveoli. Atmosphere is 0 cmH_2O. Increasing volume decreases the pressure. The lungs become negative relative to the atmosphere. Air moves from higher pressure to lower pressure. Air moves into the lungs.

By increasing the volume of a container (the lung), you reduce the pressure. By decreasing the volume of the container (the lung), you increase the pressure. The lung doesn't expand because it is filled with air. The lung is filled with air because it is expanding. The things that do the expanding are the inspiratory muscles of respiration.

When you relaxed those muscles of inspiration, when you stopped applying extra opening force, the alveoli went back to the way they started. This is called elasticity (which we discuss later in this lesson). For simplicity in this discussion, the elasticity of the lung collapses the alveoli. Without inspiratory muscles to keep them expanded (and inflated), they collapse. And the air comes out. Collapsing sounds a lot like a decreasing volume. And a decreasing volume increases the pressure in the alveoli, pushing the air out.

Take a big deep breath, hold it, then force all of the air out of your lungs. Two things happened. One, you couldn't get all the air out. If you did, your lungs would collapse, and you wouldn't be able to open them. You are not able to intuit this because you feel like you emptied all you could. (We talk about this in the pulmonary function test lesson later in the Lung series.) Two, you contracted your accessory muscles of expiration. They contract and collapse the chest wall, collapse the pleural cavity, and, most importantly, collapse the alveoli. Collapsing alveoli decrease their volume, increasing their pressure. Atmosphere is 0 cmH_2O. Collapsing the alveoli decreases their volume, increasing their pressure above 0 cmH_2O. Air moves from higher pressure to lower pressure. Air leaves the lungs.

What we just defined was the alveolar pressure. When the **alveolar pressure** is equal to the atmospheric pressure, no air moves. When alveolar pressure is less than the atmospheric pressure, air enters the lungs. When alveolar pressure is more than the atmospheric pressure, air exits the lungs. At the end of inspiration and expiration, when no air moves, the alveolar and atmospheric pressures are equal.

Anatomy of Respiration

The muscles of inspiration are those that, when they contract, increase the volume of the lung, thereby reducing pressure and drawing air into the alveoli. The **diaphragm** is the main muscle of inspiration. During quiet respiration the diaphragm is the only muscle that contracts. When it contracts, it pulls on the pleural cavity and the alveoli attached to it. All the alveoli are attached to one another, and so the diaphragm pulls all the alveoli down into the abdomen. This opens the alveoli. In addition to the diaphragm, there are **accessory muscles** of inspiration. These are the **sternocleidomastoid**, the **pectoralis minor**, and the **external intercostals**. The sternocleidomastoid lifts the sternum, increasing the volume of the lungs. The pectoralis minor lifts the ribs upward, increasing the volume of the lungs.

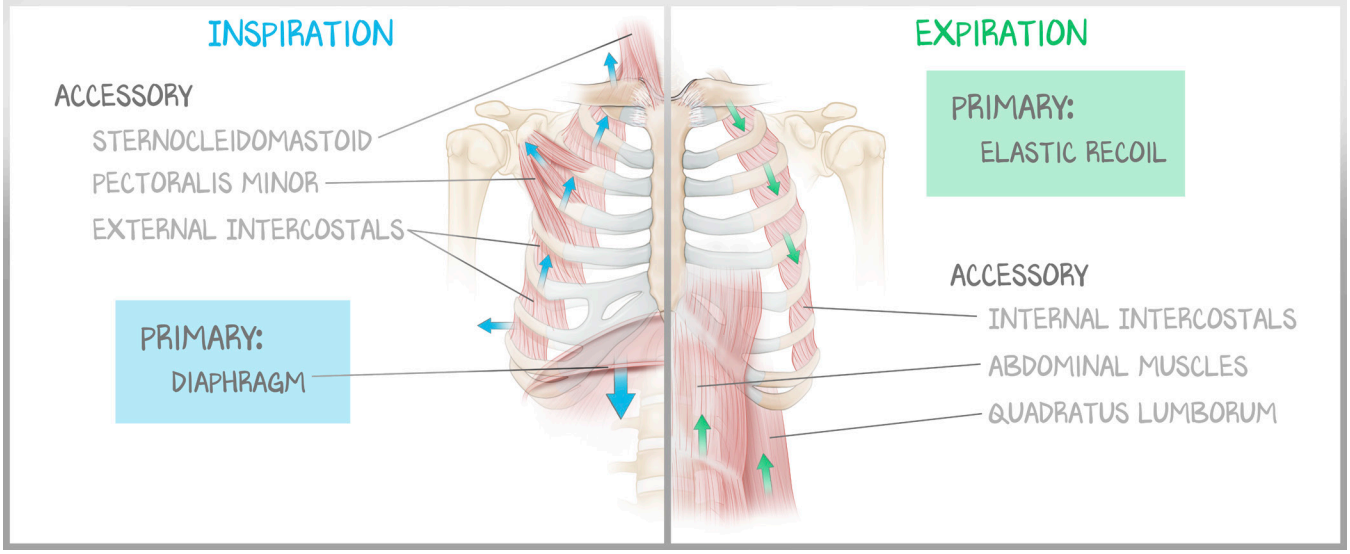

Figure 2.2: Muscles of Respiration
Muscles of inspiration pull open the chest wall and the alveoli. Increasing the volume of the alveoli decreases the pressure, and sucks in air. Muscles of expiration collapse push closed the chest wall and the alveoli. Decreasing their volume increases the pressure in the alveoli, and pushes out air. The diaphragm is the only primary muscle of inspiration, and elastic recoil of the alveoli is the primary force (it's not a muscle) of expiration. Secondary muscles are added to those used in normal quiet breathing when bigger and faster breaths are needed.

Expiration, under normal conditions, is a passive process. The **relaxation of the diaphragm** is enough to collapse the alveoli and reduce the volume of the lungs. But it isn't the relaxation of the diaphragm that does it. The diaphragm stretches out the alveoli. The more stretched out the alveoli get, the more they want to go back to being unstretched. The force that collapses the alveoli during quiet respiration is the intrinsic elasticity of the alveoli (discussed next). But sometimes the alveoli need help. The **accessory muscles** of expiration are those that decrease the volume of the lung when they contract, compressing the alveoli, forcing air out of the alveoli. These are the **abdominal muscles**, the **quadratus lumborum**, and the **internal intercostals**.

Elasticity

The definition of elastic recoil is an organ's ability to resist being deformed: if stretched out, how likely is it to return to its normal shape? Stretch out an elastic band and it gets tense. Let it go and that tension causes it to return to its original shape. Stretch that band a little, and there is only a little tension in the band, but enough to make it go back to normal when released. Stretch that band a lot, and there is a lot of tension in the band, more than enough to make it go back to normal when released. That's the elastic recoil of the elastic band. The alveoli have elastic recoil. The chest wall has elastic recoil. **Elasticity** is the

natural tendency of an organ to be a certain way. Alveoli want to collapse. In fact, if removed from the thorax, a lung will empty of air entirely, going to a volume of zero. The farther they are stretched from complete collapse, the stronger the force is to return them to collapsed.

When the lung gets stretched by the diaphragm, it fills with air. But the lung really wants to be the shape it was before the diaphragm contracted. The more stretched out the lung gets, like the elastic band, the more tension is generated. And when the alveoli stop being stretched out, the elastic recoil causes them to collapse. The reason alveoli tend to collapse is because of the presence of **elastin fibers** in the connective tissue of the alveoli. Elastin fibers want to snap back. That means the lung parenchyma itself is generating a force that favors alveolar collapse. **Exhaling**—getting air out of the lungs—is, in part, the relaxation of the diaphragm (the cessation of pull-forces expanding the lung) and, in part, the effect of elastin content in the lung (the only collapsing force in quiet respiration is due to elastin).

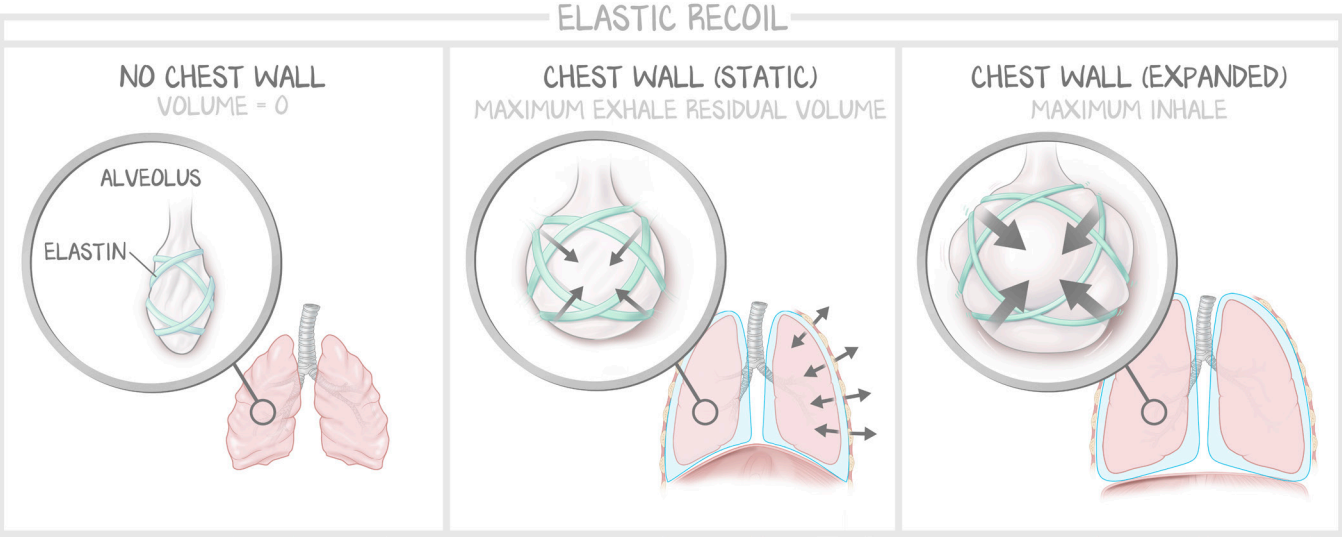

Figure 2.3: Elasticity
When the lung is taken out of the chest cavity, its volume goes to zero. That's elasticity, the elastic recoil of the alveoli. In the thorax, the alveoli do not collapse, and their volume does not go to zero (it goes to the residual volume, a subject in the next lesson). The reason is that the chest wall's elastic recoil to expand is stronger than the alveoli's elastic recoil to collapse. When you exhale as much as you can, there is still air in your alveoli. When you inhale as much as you can, the alveoli have maximum tension, so when you let go of that deep breath, the alveoli collapse. But they only collapse so far because the chest wall's elastic recoil holds them open.

Pleural Pressures

The chest wall's elastic recoil favors expansion, a pulling open of the alveoli. The elastic recoil of the alveoli favors collapse. The equilibrium is that the chest wall wins. Alveoli do not collapse because the pull by the chest wall is stronger than the pull of the alveoli. Breathing modifies the relative pressures within the alveoli, but this alteration of relative pressures does not alter this equilibrium. But the chest wall is not attached to the alveoli directly.

The chest wall is attached to the pleural cavity. It pulls outward on the pleural cavity. The pleural cavity is attached to both the chest wall and the alveoli. The outward pull of the chest wall is translated to the alveoli by the pleural cavity. The alveoli pull inward on the pleural cavity. The inward pull on the pleural cavity is translated to the chest wall. The alveoli and chest wall oppose one another. The chest wall wins. The pleural cavity feels both of these pulling forces. The pleural cavity is not connected to the atmosphere, which means it cannot change its volume. Therefore, its pressure changes instead. And since the chest wall wins, that pressure would draw air into the pleural cavity if it were connected to the atmosphere, so it must be a negative pressure within the pleural space.

The pleural cavity's pressure is called the **intrapleural pressure**. It is less than atmospheric pressure, usually around **–5 cmH_2O**. When a patient inhales, the expanding chest wall tugs on the alveoli via the pleural cavity. Alveolar volume increases. That increase in volume decreases the pressure in the alveoli, and the change in volume of the alveoli is matched by more air entering the alveoli. As the pressure gets more negative, more air fills the space. That pulling force is also felt by the pleural cavity. The chest wall has not changed its outward force. The diaphragm pulls down on the pleural cavity, adding to the opening force already exerted on the pleural cavity by the chest wall—alveolar equilibrium. Thus, the intrapleural pressure gets more negative on inspiration. Elastin fibers get more stretched out on inspiration. Therefore, on expiration, when the contraction of the diaphragm is released, the elastic recoil of the alveoli pulls on everything to restore its original volume. This compresses the alveoli and pushes air out of them. This also alleviates the extra pressure from the diaphragm on the pleural cavity, and the pleural cavity becomes less negative, back toward its baseline –5 cmH_2O.

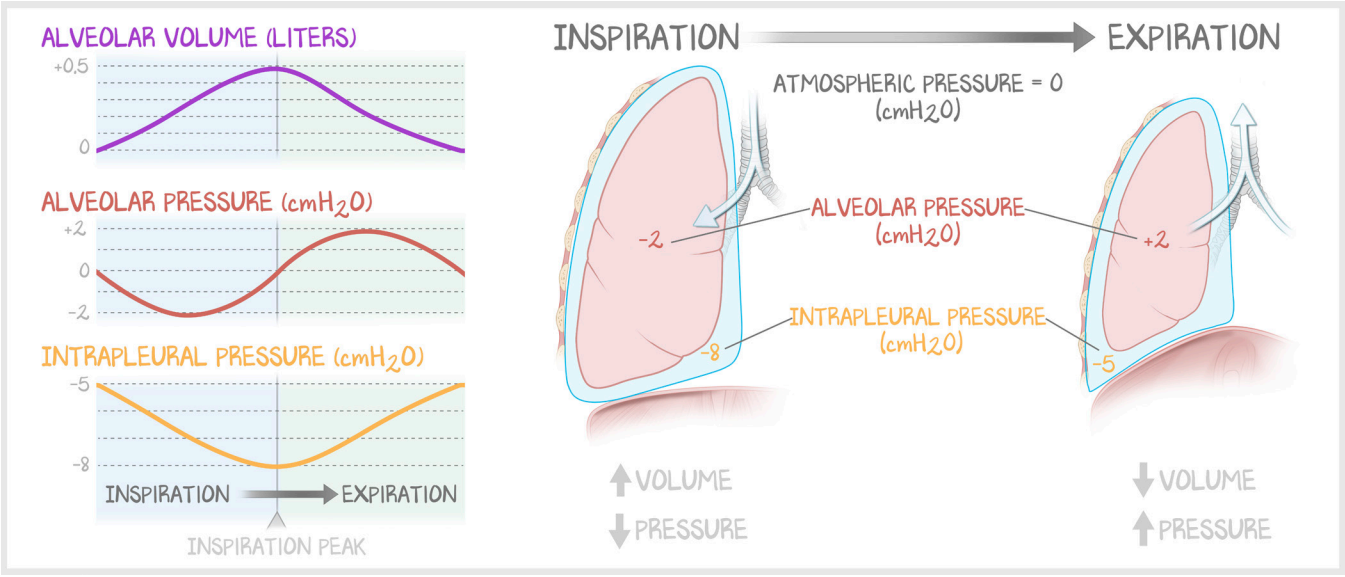

Figure 2.4: Pleural and Alveolar Pressures
As the diaphragm contracts, the alveolar volume increases, decreasing the pressure in the alveoli to below atmospheric pressure, drawing air into the lungs. In pulling on the alveoli, the diaphragm also pulls on the pleural cavity, making the pressure even more negative in the pleural cavity. The opposite is true on expiration. Air stops moving when the pressure in the alveoli is the same as the atmospheric pressure.

Dynamic Compression

Normal inspiration is to contract the diaphragm, increase the volume of the lung, thereby reducing the pressure of air, sucking air into the alveoli. Normal expiration is to release the contraction of the diaphragm, allowing the lung's elastic recoil to reduce its volume, thereby increasing the pressure and forcing air out. But the absence of diaphragmatic contraction and the elastic recoil of the lung changes the pressure only a little. The force of elastic recoil is about 10 cmH_2O. The pleural pressure in the pleural cavity upon inspiration is about –8 cmH_2O. That generates a pressure of only about 2 cmH_2O in favor of elastic recoil. A small pressure moves a small volume of air.

In a forced expiration, where pressure is generated from the contraction of expiratory muscles, the story changes. There is already the 10 cmH_2O favoring collapse from the elastic recoil inherent in the lungs. Then there is an additional pushing force generated by the contraction of those muscles. This greatly increases the pressure on the alveoli, and so greatly increases the volume that moves.

Here is why the concept of push/pull matters. The chest wall, diaphragm, and elastic recoil all pull. The accessory muscles of expiration push. The conducting airway has cartilage and doesn't change in size because of the push or pull. Alveoli are the target of these forces. Pulling them closed is the same as pushing them closed. But the **respiratory bronchioles**, the ducts through which the air must flow to exit the alveoli, do not have cartilage. On inspiration, the pull-forces **open the alveoli and respiratory bronchioles**. A larger lumen means a larger diameter, a larger diameter means less resistance, and less resistance means air flows easily. On quiet expiration, the pulling in of the alveoli does not affect the respiratory bronchioles. On forced expiration, the external push-forces from expiratory muscles **collapse the alveoli and respiratory bronchioles**. Pushing on the alveoli moves air out. But pushing on the respiratory bronchioles causes their collapse. The collapse of respiratory bronchioles decreases their diameter, increasing their resistance, **reducing airflow out**. That increased resistance, limiting airflow out, is dynamic compression and the pathophysiology behind obstructive airway disease.

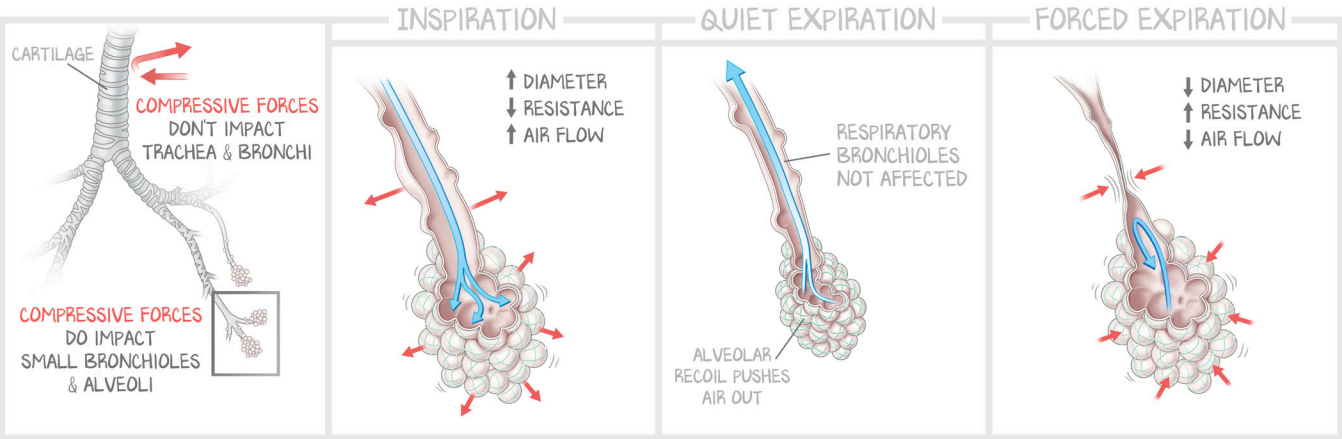

Figure 2.5: Dynamic Compression of Bronchioles
Normal quiet inspiration causes the respiratory bronchioles and alveoli to open, reducing the pressures that pull air in and also increasing the caliber of the lumen of the bronchioles, reducing resistance. Normal quiet expiration involves no external forces acting on the bronchioles. The alveoli collapse because of elastic recoil, and air moves through the bronchioles. Forced expiration has positive pressure applied that has no effect on the cartilaginous airways but is felt by respiratory bronchioles. This positive collapsing pressure is desired on the alveoli, pushing air out. However, the positive collapsing pressure on the respiratory bronchioles reduces the caliber of the lumen, increasing resistance and making it more difficult for air to move. This is a fact of forced expiration but is most poignant when discussing disease states wherein elastic recoil is lost, and external forces are required for normal ventilation (as you will see in the Obstructive Lung Disease lesson).

Surface Tension

If you spill a tiny amount of water onto your desk, you may notice it tends to bead up. Fluids do this. Water does this. It is a fact. Water has a tendency to be drawn to more water. That is called **surface tension**. Alveoli are lined with fluid. Alveoli fill with air. Alveoli are spheres that fill with air and that are lined with fluid. If that fluid were just water, the water that lines the alveoli would want to be near, be with, and coalesce with the fluid across from it in the same alveolus. This would create a force that would bring the fluid closer together, collapsing the alveoli. And the way surface tension works, the closer the water is to other water, the stronger the pulling force. That is, **the smallest alveoli have the greatest surface tension**. And, because the smallest alveoli have the smallest volume, the smallest alveoli also have the **greatest resistance to airflow**. That means the smallest alveoli are the most likely to collapse due to surface tension and the least likely to be inflated with air. The most likely to collapse are the least likely to be inflated.

To prevent that, the lungs employ surfactants. **Pulmonary surfactant** is a complex mixture of phospholipids and proteins that reduces the surface tension at the air-liquid interface of the alveolus.

Surfactant is mostly **dipalmitoylphosphatidylcholine**, an amphipathic molecule with a hydrophilic head and long hydrophobic tail. The hydrophilic heads are inserted into the fluid lining the alveoli. The hydrophobic tails are oriented toward the air space. As the alveolus decreases in size, the hydrophobic tails get closer to the liquid on the alveolus across from them. The water pulls the alveoli closed (surface tension), but the hydrophobic tails repel the water (opposes surface tension). As the alveoli get smaller, the surface tension increases. As the alveoli get smaller, the repelling force of the hydrophobic tails also increases. **Type 2 pneumocytes** produce surfactant.

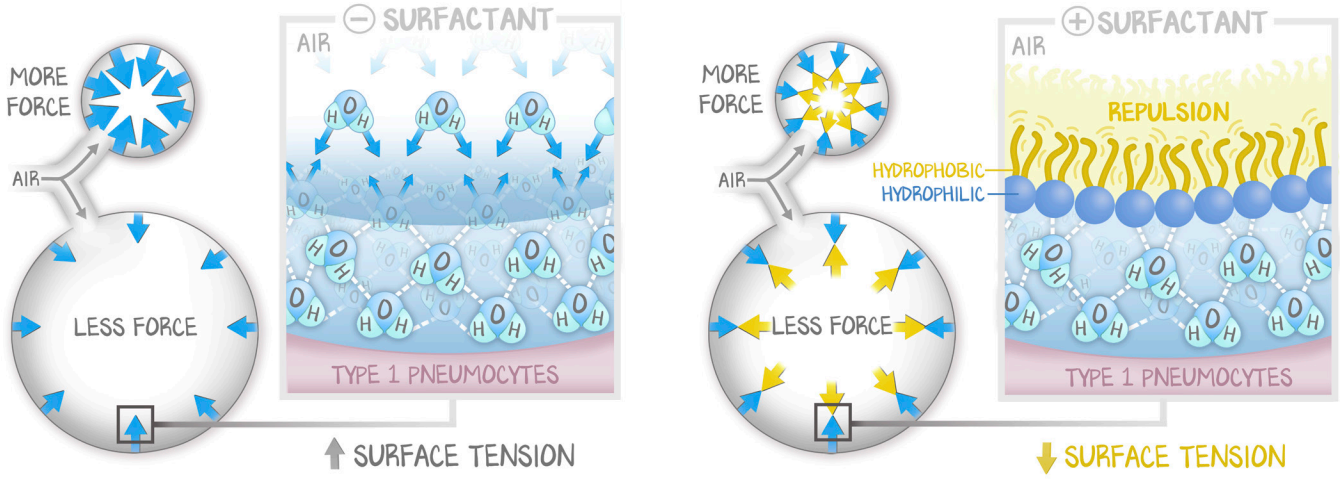

Figure 2.6: Surface Tension
Surface tension is the reason it is easy to quickly blow out a lot of air after maximal inspiration, and also why it is hard to quickly inhale a lot of air after maximal expiration. With maximal expiration, the alveoli collapse. The sphere filled with air and lined with liquid (the alveolus) gets smaller in diameter. The liquid gets closer to other liquid, and surface tension favors more collapse. That surface tension must be overcome by the contraction of the diaphragm. When it is overcome, the alveoli open. At maximal inspiration, the alveoli are as filled with air as possible. The liquid lining the air-filled spheres is the farthest from other liquid. Surface tension is lowest, and expiration opposes neither the force of elastic recoil nor surface tension—they work together to get the air out.

A normal, healthy lung does not have collapsed alveoli. The chest wall's elastic recoil keeps them filled with air, and the surfactant opposes surface tension. Surface tension is only a problem in pathologic states. Surface tension is what compromises lung compliance, discussed next.

Compliance

If you blow into a balloon, the balloon changes shape easily. That is, it distends, changing its volume a lot with little effort. That balloon has high compliance. If you blow into a steel flask, the steel flask does not change shape easily. That is, it does not change its volume even with a lot of effort. The steel flask has low compliance.

The lungs are supposed to be compliant. Only a small change in alveolar pressure is necessary to change the alveolar volume. Or rather, the diaphragm doesn't have to work very hard to make a change in volume that reduces the pressure in the alveoli during inspiration. Normal alveoli easily fill with air. And, in return, the alveoli are quite elastic. Easy to open, easy to close. **Collapsed alveoli are hard to open.** Collapsed alveoli have very low compliance. The chest wall's elastic recoil helps prevent the complete collapse of alveoli from without, opposing alveolar elasticity. Surfactant prevents the collapse of alveoli from within, opposing surface tension. But if some alveoli do collapse, surface tension keeps them closed, and the high resistance to airflow prevents their reinflation. Alveolar collapse is seen in **pulmonary edema**, especially in the pathogenesis of ARDS.

Alveolar collapse is not the only thing that can affect compliance. **Pulmonary fibrosis** also causes reduced compliance. Collagen is not elastic. In fact, it is the opposite. It is rigid and stiff. Fibrosis is the deposition of collagen. If collagen is added to the septa or alveoli, they will be less likely to open.

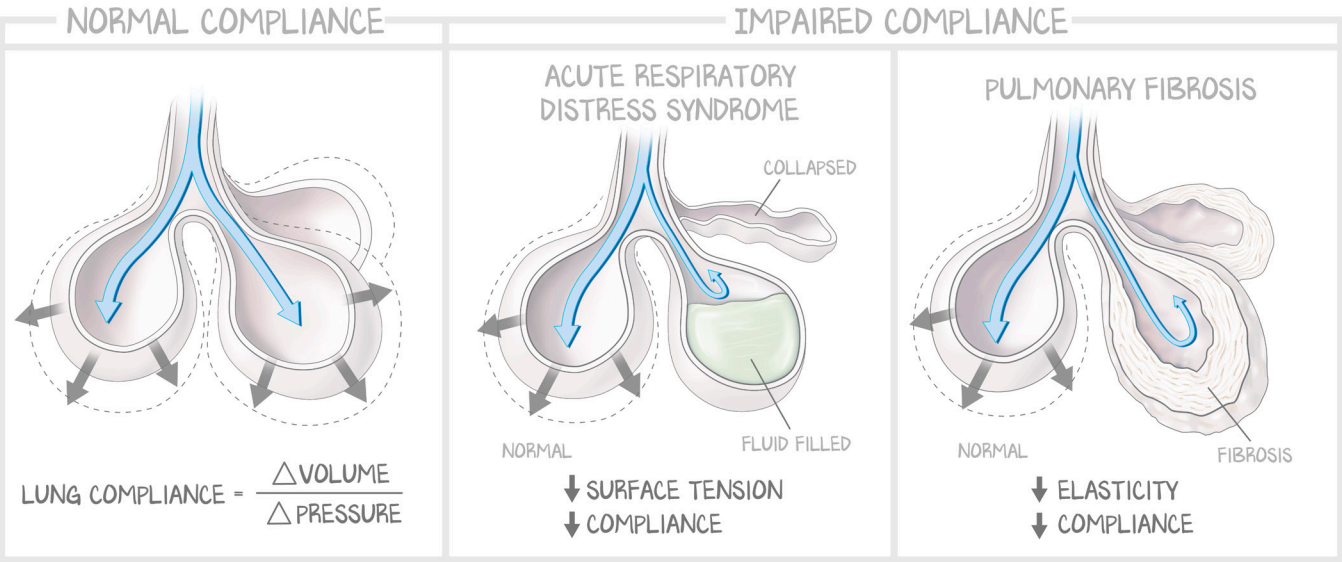

Figure 2.7: Compliance
(a) A normal lung is very compliant. A small change in pressure is required to make the lung larger and, therefore, pull in air. These alveoli are unimpeded by fluid or fibrosis. (b) In pulmonary edema, the alveoli are impeded by fluid. The amount an alveolus can be filled remains unchanged (the septa are normal), but instead of having that volume be filled with air (which moves easily, so is compliant), that volume is now filled with fluid (which is noncompliant). (c) In pulmonary fibrosis, the alveoli are impeded by fibrosis. Fibrosis replaces the compliant alveolar septa with more rigid collagen. In this case, it isn't the substance filling the alveolar volume, it is something stiff inside the septa.

Regulation of Respiration

We've talked about the push- and pull-forces that move air. We've talked about elasticity and compliance. We've talked about the mechanics and the physics of a single breath. But what regulates breathing? What regulates how fast or how deep our breathing is? A person does not need to attend to respiration to continue respiring. That is because our respiratory rate is controlled by our autonomic nervous system. We can consciously vary our respiratory rate—voluntarily hold our breath or breathe more quickly—but a human cannot will the complete arrest of breathing.

Respiration is managed in the **medulla**, where the dorsal respiratory group and the ventral respiratory group are located.

The **dorsal respiratory group** (DRG) is the pacemaker for inspiration and has most of its neurons in the nucleus tractus solitarius. It is the inspiration center. Even when all inputs to the DRG are sectioned and the medulla transected above and below the DRG, the DRG neurons sustain a regular rhythmic pattern of discharge and senescence. The intrinsic respiratory rate is 12 breaths per minute. When the DRG fires, the **phrenic nerve** stimulates the diaphragm to contract (inspiration). When the DRG is quiet, the phrenic nerve doesn't stimulate the diaphragm and it relaxes (expiration). The DRG also has inputs to other accessory muscles of inspiration. Therefore, all the neurons from the DRG are said to be **inspiratory neurons**—their firing induces contraction of the muscles of inspiration.

The **ventral respiratory group** (VRG) does not participate in the normal oscillating rhythmic pattern of respiration. Quiet respiration is a combination of **active** diaphragm contraction, **inactive** diaphragm relaxation (DRG fires and stops, respectively), and the **passive** elastic recoil of the lungs. The VRG kicks on when additional muscles are required. VRG activity increases **both** inspiration and expiration muscles, so it has a combination of **inspiratory and expiratory neurons**. The VRG is activated when a person needs to breathe harder and faster. Thus, this area operates more or less as an overdrive mechanism when high levels of pulmonary ventilation are required, especially during heavy exercise.

The pons modulates, but is not essential for, normal respiration. The pons is where the pneumotaxic and apneustic centers are found. Although lesions of these centers do result in abnormal breathing in animal studies, altering other experimental parameters (such as heat) can reverse the findings of the lesion. So, although the apneustic and pneumotaxic centers do help in smoothing out the respiration, they are now generally considered only of historical significance.

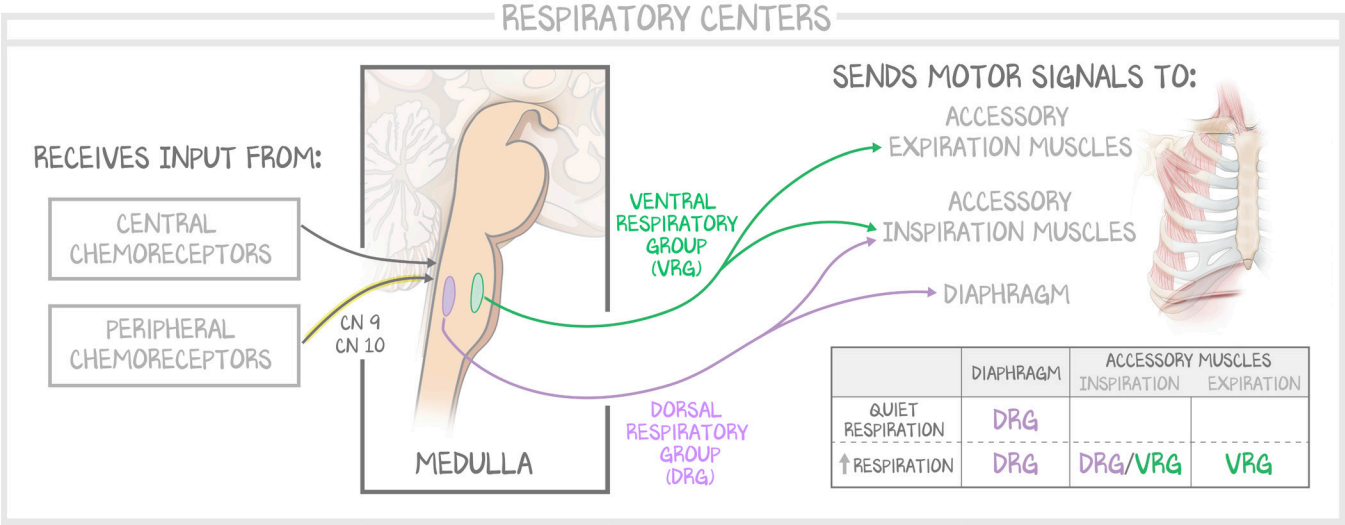

Figure 2.8: Respiratory Centers of the Brain
The dorsal respiratory group of the medulla is responsible for output to the diaphragm via the phrenic nerve, made of C3, C4, and C5. DRG output is 12 inhalations per minute. When more inspiratory effort is needed, the DRG can also trigger the accessory muscles of inspiration. When any help is needed with expiration or when more inspiratory effort is needed, the VRG kicks on. The pons participates in, but does not control, inspiration or expiration.

So, we know the outputs come from the DRG normally and the VRG when more breathing is needed, and the pons doesn't regulate the rate or depth of respiration. So, what does regulate the output of the DRG and VRG? That would be the chemoreceptors—central and peripheral.

The **central chemoreceptor** is found in the **medulla**, in the ventrolateral medulla, separate from any of the regions discussed so far. It responds to **cerebrospinal fluid H^+ concentration**. It uses CO_2 in the CSF as a surrogate for the acidity of the blood. How is explored in Figure 2.9 in broad strokes, and in greater detail in the next lesson. Effectively, CO_2 diffuses through the blood-brain barrier into the CSF, where carbonic anhydrase converts it and water to H^+ and HCO_3^-, which, being charged, cannot leave through the blood-brain barrier. The more CO_2 in the blood, the more CO_2 in the CSF, the more substrate to be turned into H^+. As H^+ rises, the pH drops. A rise in blood CO_2 results in an increased respiratory rate, blowing off CO_2; a decrease in blood CO_2 results in a decreased respiratory rate, holding onto CO_2. **The goal of the central chemoreceptor is to adjust CO_2 in the blood to sustain a normal blood pH.**

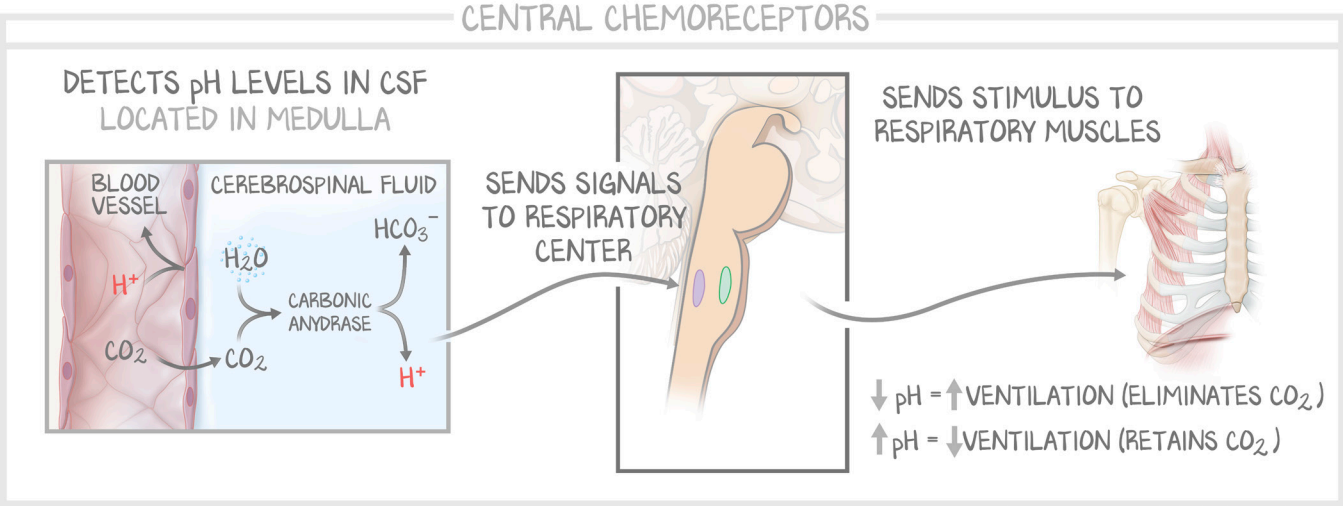

Figure 2.9: Central Chemoreceptors
The central chemoreceptors assess and respond to the level of CO_2 in the blood; they both increase respiration to reduce CO_2 and decrease respiration to increase CO_2. They directly assess the CSF for H^+ ions, the surrogate for CO_2, because H^+ is a product of carbonic anhydrase's joining of CO_2 with water.

The **peripheral chemoreceptors** are found in the **carotid bodies** (carried along the glossopharyngeal nerve) and the **aortic body** (carried by the vagus nerve). These are the same bodies you saw in Cardiology that acted as baroreceptors. In response to **hypoxemia**, these neurons increase their firing rate, stimulating respiration. There is a linear dose-response curve for low oxygen levels—the lower the oxygen goes, the faster the respiratory rate gets and the larger the inspirations become. However, giving excess oxygen (pushing the partial pressure of oxygen in the blood to above 100 mmHg) does not reduce the respiratory rate below the baseline. This **hypoxemic drive** stimulates respiration to restore oxygen levels, but once restored does not influence respiratory rates.

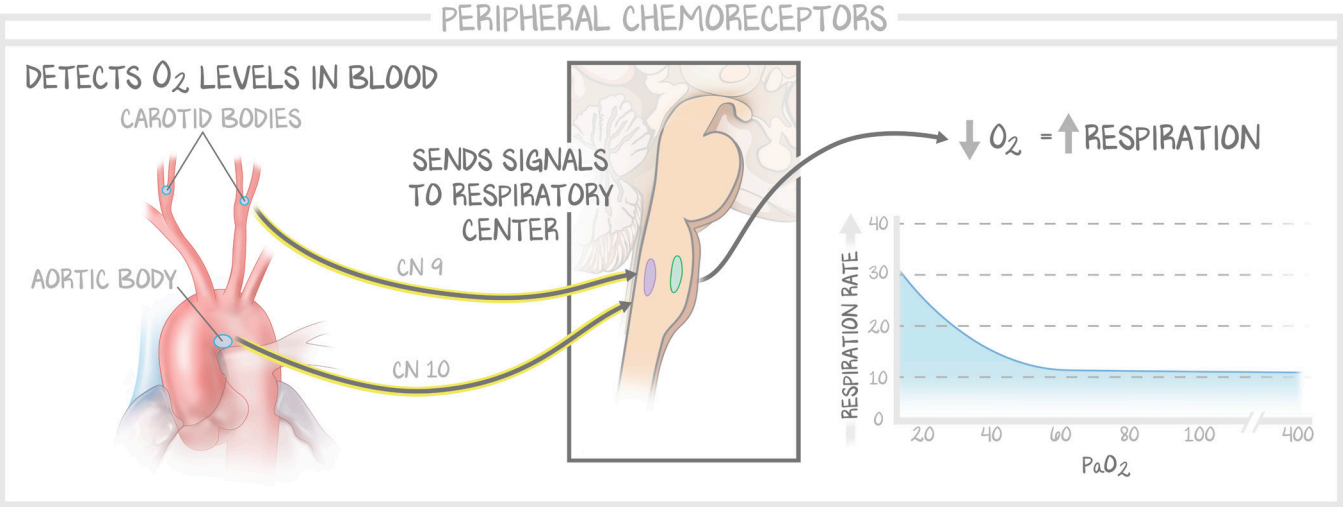

Figure 2.10: Peripheral Chemoreceptors
Peripheral chemoreceptors assess the blood for oxygen and increase respiration when oxygen levels fall. There is no inhibition of respiration when oxygen levels rise. Although the peripheral chemoreceptors also respond to CO_2 and pH, we want you to learn, *"central CO_2, peripheral O_2."*

Other Things That Affect Respiratory Rate

Humans can exert **voluntary** control over breathing, the signal coming from the cortex. For example, you can hold your breath while you go underwater, and a powerful singer can sustain a note longer than some humans can simply exhale.

Humans are also vulnerable to **hypothalamic** inputs, such as when fear, pain, and anxiety increase the respiratory rate.

Some other things are considered lower-yield. They should be seen as protective measures that aren't activated day to day. The **Hering-Breuer stretch reflex** cuts off inspiration when a certain volume is reached. Under normal conditions, the volume at which this reflex terminates inspiration is 1500 mL (normal breathing is 500 mL), so this reflex does not contribute to regular respiration. **J receptors** are intra-alveolar nerve endings that respond to edema. Although their function is not well elucidated, it is thought that they contribute to the sensation of dyspnea even in the absence of hypoxemia. **Irritant** receptors inhibit inspiration when irritants enter the nasopharynx (cigarette smoke, pollen, etc.) and induce cough. These things are not what regulate breathing but are involved in the lung.

Vocabulary

Inspiration and inhalation are the same thing. Exhalation and expiration are the same thing. You can find some forms of inspiration inspiring, but that is not inhalation. When a person expires, it means they are dead, which is also not expiration. For pulmonary, inspiration and inhalation will be used interchangeably, as will exhalation and expiration.

Lactate and lactic acid mean the same thing. They are used interchangeably throughout our curriculum on purpose.

Human respiration is the pattern of inhalation and expiration (see what we did there?). Cellular respiration is the using of oxygen and glucose to make carbon dioxide and ATP. Cellular respiration requires aerobic conditions. Cells undergoing cellular respiration are using oxygen. Anaerobic conditions (low oxygen in tissues) results in anaerobic metabolism—glucose is consumed, but no oxygen is used and no carbon dioxide forms; lactate does instead.

We're going to intentionally switch between -spiration and -halation because they are used so often interchangeably elsewhere. When we mean human respiration, we're going to say just "respiration." When we mean the cell is performing cellular respiration in the presence of oxygen and glucose, we'll say "cellular respiration" (always together). When we mean to communicate that the output of a cell's need for ATP will be lactic acid, we'll say "anaerobic metabolism."